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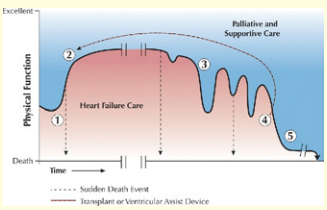
QUARTERLY FOCUS ISSUE: HEART FAILURE



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HEART FAILURE WITH PRESERVED EJECTION FRACTION

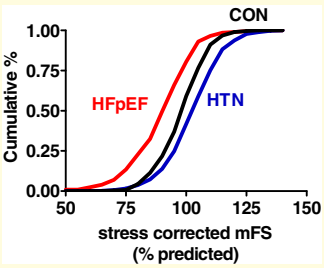
HFpEF Associated With Reduced Myocardial Energy Reserve 402

Thanh T. Phan, Khalid Abozguia, Ganesh Nallur Shivu, Mahadevan Gnanadevan, Ibrar Ahmed, Lynne Williams, Girish Dwivedi, Kiran Patel, Paul Steendijk, Houman Ashrafian, Anke Henning, Michael Frenneaux

Phan and colleagues performed magnetic resonance spectroscopy and radionuclide ventriculography at rest and during exercise in patients with heart failure with preserved ejection fraction (HFpEF) and healthy control patients. At rest, the time to peak left ventricular filling (nTPPF) was similar in patients and control patients; however, the cardiac creatine phosphate/adenosine triphosphate ratio was reduced in HFpEF subjects, indicating reduced energy reserves. There were smaller augmentations in stroke volume during submaximal exercise in HFpEF subjects, and nTTPF fell during exercise in control patients but increased in HFpEF patients. Integrating these observations, the authors speculate that dynamic energy impairment may account for the slowing of left ventricular (LV) active relaxation during exercise as well as the failure of LV contractile function to increase.

HEART FAILURE WITH PRESERVED EJECTION FRACTION

Ventricular Systolic Stiffening May Underlie HFpEF 410



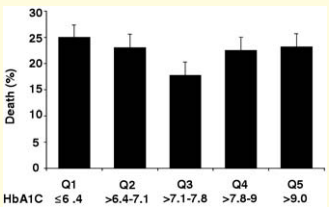
Barry A. Borlaug, Carolyn S. P. Lam, Véronique L. Roger, Richard J. Rodeheffer, Margaret M. Redfield

Borlaug and colleagues provide insights into the systolic function of patients with heart failure with preserved ejection fraction (HFpEF) using detailed echocardiographic studies of healthy control patients, hypertensive control patients without heart failure, and subjects with HFpEF. Load-independent indexes of chamber-level contractility (pre-load recruitable stroke work and wall stress-corrected endocardial fractional shortening) and of myocardial contractility (stress-corrected midwall fractional shortening) were found to be higher in the hypertensive subjects than in control patients, but lower in those with HFpEF. These findings indicate that in spite of the apparently "preserved" ejection fraction, patients with HFpEF do have impaired contractile function.

Editorial Comment: Samer S. Najjar, p. 419

HEART FAILURE AND DIABETES

Retrospective Study Suggests That Optimal HbA1C Level is 7% to 8% for Patients With HF 422



David Aguilar, Biykem Bozkurt, Kumudha Ramasubbu, Anita Deswal

There is clear evidence that high glucose levels can be detrimental to cardiac function, but other studies have suggested that tight glucose control may increase mortality. Aguilar and colleagues reviewed data from almost 6,000 subjects with a history of both heart failure (HF) and diabetes. The risk of subsequent death or HF hospitalization was then compared with levels of glycosylated hemoglobin (HbA1C). At 2-year follow-up, the adjusted risk for death was about 25% lower for those with a HbA1C 7.1% to 7.8%, compared with those with either higher or lower values. The association between mortality and HbA1C in diabetic patients with HF appears U-shaped, with the lowest risk of death in those patients with modest glucose control.

Editorial Comment: Larry A. Weinrauch, Eldrin F. Lewis, p. 429

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HEART FAILURE AND GENETICS

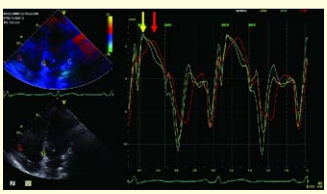
Survival Benefit of Beta-Blockers Modified by Genetic Polymorphisms 432

Sharon Cresci, Reagan J. Kelly, Thomas P. Cappola, Abhinav Diwan, Daniel Dries, Sharon L. R. Kardia, Gerald W. Dorn II

Some studies have suggested that the benefits of β-blocker therapy in patients with heart failure (HF) may not be seen in African Americans. Cresci and colleagues hypothesized that this is due to different frequencies of 2 polymorphisms in the beta-adrenergic system. Almost 2,500 subjects with HF were genotyped for the β1-adrenergic receptor (ADRB1) Arg389>Gly and G-protein receptor kinase 5 (GRK5) Gln41>Leu polymorphisms. As expected, these polymorphisms were more prevalent among African Americans, and β-blocker treatment increased survival in Caucasians but not African Americans. Further analysis showed that ADRB1 Gly389 was associated with decreased survival and GRK5 Leu41 with improved survival. Subjects with the combination ADRB1 Gly389 GRK5 Gln41Gln had a similar benefit from β-blocker therapy regardless of race, confirming that genetic differences in the β-adrenergic receptor signaling pathway underlie the apparent differences seen in African Americans and Caucasians.

RIGHT VENTRICULAR CARDIOMYOPATHY

Arrhythmogenic RV Dysplasia/Cardiomyopathy May Cause Ventricular Dyssynchrony 445



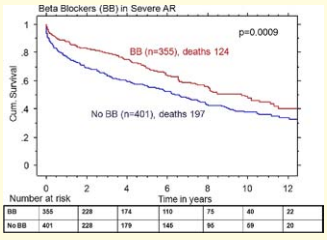
Laurens F. Tops, Kalpana Prakasa, Harikrishna Tandri, Darshan Dalal, Rahul Jain, Veronica L. Dimaano, David Dombroski, Cynthia James, Crystal Tichnell, Amy Daly, Frank Marcus, Martin J. Schalij, Jeroen J. Bax, David Bluemke, Hugh Calkins, Theodore P. Abraham

Tops and colleagues studied the prevalence and mechanisms underlying right ventricular (RV) dyssynchrony in subjects with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) using tissue Doppler echocardiography (TDE). Mechanical synchrony was assessed by measuring differences in time-to-peak systolic velocity (TSV) between the RV free wall, ventricular septum, and left ventricular lateral wall. RV dyssynchrony was present in one-half of the ARVD/C subjects; these subjects had a larger RV end-diastolic area and lower RV fractional area change compared with ARVD/C patients without RV dyssynchrony. RV dyssynchrony may occur in ARVD/C patients, and is associated with RV remodeling.

CLINICAL RESEARCH

VALVULAR HEART DISEASE

Beta-Blockers May Improve Outcomes in Patients With Severe AR 452



Unnati Sampat, Padmini Varadarajan, Rami Turk, Ashvin Kamath, Sumit Khandhar, Ramdas G. Pai

Beta-blockers (BBs) are thought to be contraindicated in patients with severe aortic regurgitation (AR) because slower heart rates increase the duration of diastole during which AR occurs. Yet, the neuroendocrine activation with AR is similar to that seen with systolic dysfunction. Sampat and colleagues reviewed a large echocardiographic database and identified almost 800 subjects with severe AR. Nearly one-half of the subjects were on a BB. With a mean duration of follow-up 4.5 years, BB use was associated with higher survival rates at 1 and 5 years, and was an independent predictor of better survival. This observational study suggests that BB therapy may improve survival in patients with severe AR.

Editorial Comment: Uri Elkayam, p. 458

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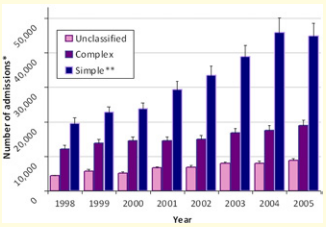
CONGENITAL HEART DISEASE

Increasing Numbers of Hospitalizations for Adults With CHD 460

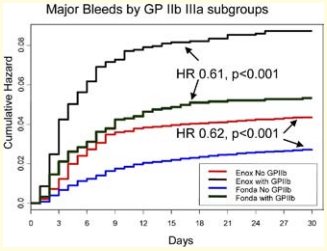


Alexander R. Opotowsky, Omar K. Siddiqi, Gary D. Webb

Over the last 50 years, the life expectancy of patients with congenital heart disease (CHD) has greatly increased. Opotowsky and colleagues identified patients ≥18 years of age admitted to an acute care hospital with an International Classification of Diseases-Ninth Revision code designating a CHD diagnosis. The number of adult CHD hospitalizations increased 100% from 1998 to 2005. Mean hospital charges per hospitalization rose 127%, and the estimated total national charges for these hospitalizations increased 357% to $3.16 billion. The number of hospital admissions for adults with CHD in the U.S. more than doubled between 1998 and 2005, and the costs of these hospitalizations almost quadrupled.

ACUTE CORONARY SYNDROMES

Fondaparinux Reduces Bleeding Compared With Enoxaparin 468

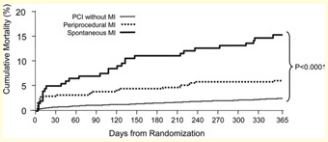


Sanjit S. Jolly, David P. Faxon, Keith A. A. Fox, Rizwan Afzal, William E. Boden, Petr Widimsky, P. Gabriel Steg, Vicent Valentin, Andrez Budaj, Christopher B. Granger, Campbell D. Joyner, Susan Chrolavicius, Salim Yusuf, Shamir R. Mehta

The OASIS 5 trial demonstrated that fondaparinux reduced major bleeding by 50% compared with enoxaparin while preserving similar efficacy in reducing ischemic outcomes. Jolly and colleagues performed this retrospective subgroup analysis to determine if this benefit is affected by concurrent antiplatelet therapy with clopidogrel and/or glycoprotein (GP) IIb/IIIa inhibitors. Subjects in the trial were randomized to either fondaparinux or enoxaparin, but the use of GP IIb/IIIa inhibitors or thienopyridines was at the discretion of the treating physician. There was a 40% reduction in major bleeding with fondaparinux in those treated with GP IIb/IIIa (hazard ratio [HR]: 0.61) and a similar reduction in those treated with thienopyridines (HR: 0.62). In patients receiving GP IIb/IIIa inhibitors or thienopyridines, fondaparinux reduces major bleeding and improves net clinical outcome compared with enoxaparin.

ACUTE CORONARY SYNDROMES

Periprocedural MI Does Not Significantly Affect Outcomes 477



Abhiram Prasad, Bernard J. Gersh, Michel E. Bertrand, A. Michael Lincoff, Jeffrey W. Moses, E. Magnus Ohman, Harvey D. White, Stuart J. Pocock, Brent T. McLaurin, David A. Cox, Alexandra J. Lansky, Roxana Mehran, Gregg W. Stone

This study by Prasad and colleagues evaluated the relative impact of periprocedural and spontaneously occurring myocardial infarction (MI) on survival following percutaneous coronary interventions (PCIs). Subjects in the ACUITY trial were examined for periprocedural MI, defined as a rise in creatine kinase-myocardial band within 24 h post-PCI, and spontaneously occurring MI, which was not procedure-related and occurred within the first year after enrollment. A periprocedural MI developed in 6.0% and a spontaneously occurring MI developed in 2.6%. Patients developing spontaneously occurring and periprocedural MIs had significantly higher unadjusted rates of mortality. After adjusting for differences in baseline and procedural characteristics, spontaneously occurring MI was a powerful independent predictor of subsequent mortality (hazard ratio: 7.5), whereas periprocedural MI was not. Among patients with acute coronary syndromes undergoing PCI, periprocedural MI is a marker of baseline risk, atherosclerosis burden, and procedural complexity, but does not have independent prognostic significance.